

REMARKS

Applicants acknowledge with appreciation receipt of the Notice of Allowance mailed August 11, 2003. By this Amendment, Claim 36 is being amended, and no claims are being added or canceled. Therefore, Claims 30-31, 35-40 and 44-47 are pending in the application.

This Amendment is being submitted concurrently with a Request for Continued Examination ("RCE"), an Information Disclosure Statement ("IDS"), a Substitute Form PTO-1449A and copies of the listed references and/or information. The IDS is intended to make of record various papers that have arisen in the course of legal proceedings in Japan and Europe.

The Amendments of the Claims

Claim 36 has been amended to correct an obvious error in antecedent basis. As amended, Claim 36 recites an instrument that includes a sealed transmission path between the reaction vessel and the detector. Support for amendment is found in the specification at, for example, page 14, lines 24-34; page 28, line 34 through page 29, line 9; and in FIG. 7, which illustrates a fiber optic embodiment of a sealed transmission path. Accordingly, no new matter is introduced by virtue of the amendment.

Concurrently Filed IDS

The enclosed IDS discusses the origins of various references that have been cited in legal proceedings involving counterpart Japanese or European patents. Three particular references are addressed further below.

European Patent application EP 0 487 218 A2 (Cite No. 25) published on May 27, 1992, and therefore does not qualify as prior art against the instant application, which has an effective filing date of May 2, 1991. Furthermore, the corresponding U.S. application Serial No. 07/784,888 was involved in an interference with parent application Serial No. 07/695,201, now U.S. Patent No. 5,994,056 (Interference No. 103489), in which the parent '201 application was awarded priority.

Cite No. 41 corresponds to the cover page, title page and pages i-iii, 1, 2, 48-56 and 65 of Eigen et al., "Report on Evolution Research," Department of Biochemical Kinetics, Max Planck Institute für Biophysikalische Chemie ("Eigen Report"), which were brought to the attention of the Japanese Patent Office in a Japanese counterpart of the instant application (Japanese Patent

No. 3136129). Cite No. 41 contains pages of the Eigen Report in addition to those that have already been made of record in the instant application in a Supplemental Information Disclosure Statement filed July 19, 2001 (Cite No. 19).

This reference was purportedly made publicly available April 18-20, 1991 at a meeting or conference at the Max Planck Institute in Göttingen, Germany, according to declarations submitted during prosecution of European Patent EP 0 583 265 (see English translations of declarations by M. Eigen, R. Winkler-Oswatitsch, B. F. Lindemann, A. Schwienhorst and R. Günther, Cite No. 42). However, this reference cannot qualify as prior art, because its alleged publication date was less than one year before the effective filing date of the present application, and because the presently claimed invention was actually reduced to practice prior to the alleged publication date.

As evidenced by the enclosed Declaration of inventor Russell G. Higuchi Under 37 CFR § 1.131 ("Higuchi Declaration;" attached hereto as Exhibit 1), an embodiment of the instantly claimed instrument was actually reduced to practice before April 15, 1991, which is before the alleged publication date of April 18-20, 1991 of Cite No. 41. As is apparent from ¶5 of the Higuchi Declaration, an instrument in accordance with the present claims was used to monitor a polymerase chain amplification reaction in real time. The specific instrument used included a thermal cycler adapted to receive at least one reaction vessel and a detector operable to detect, by way of an optical fiber, a fluorescence signal while the amplification was in progress and without having to open the reaction vessel. The reaction vessel in which the polymerase chain amplification reaction was carried out contained an amplification mixture comprising a target nucleic acid, reagents for nucleic acid amplification and a detectable nucleic acid binding agent (ethidium bromide). The trace of the results of the experiment (attached as Exhibit A to the Higuchi Declaration), which Dr. Higuchi received and understood before April 15, 1991, demonstrates that the instrument worked for its intended purpose.

Applicant notes that while it has opted to antedate the alleged publication date of Cite No. 41, Applicant has in no way admitted or conceded that: (1) Cite No. 41 anticipates and/or obviates the Claims; (2) that Cite No. 41 constitutes a printed publication; and/or (3) that, if Cite No. 41 constitutes a printed publication, it published prior to the effective filing date of the instant application. Applicant expressly reserves the right to address any or all of these issues at a later date.

Cite No. 47 is an Annex (Annex 2) reproduced from Cite No. 46 (opposition brief submitted by Eppendorf). The Annex purports to describe an experiment performed using a system that allegedly corresponds to a measuring station Eppendorf has sold since the 1970's, called a Measuring Station 5086 (described in Cite No. 30). However, it is evident that significant modification to Measuring Station 5086 was required for the experiment to be carried out.

The system used for the experiment, illustrated in FIG. 1 of Annex 2, included an Eppendorf Photometer 1101 with fluorescence attachment 1030, a mercury lamp and two thermostatted water baths (Eppendorf thermostats 2762 and 2763), filled with 1.2 and 3 liters of water, respectively, tempered to 96°C and 5°C, respectively. The water baths were connected to the tempering device of the fluorescence attachment by silicone tubing (see Cite No. 47 at page 2).¹ The system also included an analog recorder (Cite No. 47 at page 2, ¶5).

This system was used to monitor a PCR reaction carried out in the presence of SYBR® Green fluorescent dye (Cite No. 47 at Section 3.2). However, this experiment did not utilize the Measuring Station 5086 as originally disclosed. In particular, the two-bath system used in the experiment in Cite No. 47 does not correspond to the single-bath Measuring Station 5086 (see Cite No. 30) as alleged (see Cite No. 47 at page 2, ¶1). Cite No. 47 also alleges that the experiment could have been carried out with a single water bath instead of two water baths, but that this would have "taken longer" (see Cite No. 47 at page 2, ¶4). However, such an assertion is both misleading and irrelevant since the actual Measuring Station 5086 (as advertised and sold commercially) did not include a thermocycler at the time of the present invention. Accordingly, Cite No. 47 is without merit.

Conclusion

It is respectfully submitted that Claims 30-31, 35-40 and 44-47 satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same is therefore kindly requested.

¹ All references to Cite No. 47 are to the English translation except as to Figures.

No fees beyond those included with the enclosed RCE transmittal are believe to be due in connection with this Amendment. However, the Patent Office is authorized to take any required fees from Applied Biosystems Deposit Account No. 01-2213 (Order No. 4380US).

Respectfully submitted,

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Vincent M. Powers

Vincent M. Powers
Attorney for Applicant
Reg. No. 36,246
Telephone: 650-638-6492

CORRESPONDENCE ADDRESS

Customer Number 22896
Applied Biosystems
850 Lincoln Centre Drive
Foster City, California 94404
TEL: 650-570-6667
FAX: 650-638-6677